RESULTS

Baseline Characteristics

- Fifteen subjects were enrolled in China between September 2002 and February 2003. All subjects were Asian, genotype C or D, and HBeAg positive. Consistent with this patient population, subjects were young with high HBV DNA, RNA and HBeAg levels at baseline. Notably, nearly half of subjects (53%) had normal alanine aminotransferase (ALT) levels at baseline.

Table 1: Baseline characteristics and Demographics

| Characteristic | N | Mean ± SE | Median
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<tbody>
<tr>
<td>Age, years (SE)</td>
<td>15</td>
<td>40.3 ± 0.3</td>
<td>40</td>
</tr>
<tr>
<td>Sex (Male/Female)</td>
<td>15</td>
<td>10/5</td>
<td>10/5</td>
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<tr>
<td>Race (Asian)</td>
<td>15</td>
<td>15</td>
<td>15</td>
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<tr>
<td>HBV Genotype</td>
<td>15</td>
<td>B: 9 (60%), C: 6 (40%)</td>
<td>B: 9 (60%)</td>
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<tr>
<td>ALT U/L</td>
<td>15</td>
<td>55.3 ± 9.3</td>
<td>60</td>
</tr>
<tr>
<td>HBV DNA log(10) IU/mL</td>
<td>15</td>
<td>6.2 ± 0.2</td>
<td>6.5</td>
</tr>
<tr>
<td>HBeAg log(10) ng/mL (mean, SEM)</td>
<td>15</td>
<td>4.2 ± 0.2</td>
<td>4.2</td>
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<tr>
<td>ALT ULN, mean (SEM)</td>
<td>15</td>
<td>40.3 ± 0.3</td>
<td>40</td>
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Subject Disposition

- Dosing ongoing: N=12 (80%); median duration of dosing: 232 days
- Dosing prematurely stopped: N=3 (20%) due to safety-related personal reasons (N=2) and confirmed non-compliance beginning at Week 12 (N=1)
- Safety
  - 300 mg ALG-000184 + 0.5 mg ETV for up to 36 weeks was generally well tolerated.

Table 2: Summary of Treatment Emergent AEs (TEAEs)

| TEAEs leading to study drug discontinuation | 0 |
| Subjects with Grade 3 TEAEs | 0 |
| Subjects with Grade 4 TEAEs | 0 |

Pharmacokinetics

- Plasma ALG-001075 accumulation at Week 12 was ~60%.
- PK was generally similar compared to a prior cohort given 300 mg ALG-000184 alone, suggesting no impact of ETV on ALG-000184 exposures.
- ETV exposures were similar with or without ALG-000184 co-administration.

Antiviral Activity: HBsAg

- HBsAg declined steadily on treatment in the majority of subjects (Figure 3).
  - Specific dosing with ALG-000184 + ETV.
  - HBsAg declined by:
    - ≥ 0.5 log(10) IU/mL in 7/12 subjects dosed for 12 weeks
    - ≥ 1.0 log(10) IU/mL in 47 subjects dosed for 24 weeks
  - Maximum HBsAg decline observed to date: 2.4 log(10) IU/mL (Week 36)
  - Two (2) of 3 subjects originally receiving placebo + ETV experienced more substantial HBsAg reductions after adding on ALG-000184 at Week 12.

Antiviral Activity: HBV DNA and HBV RNA

- The addition of 300 mg of ALG-000184 at Week 12 in subjects initially receiving ETV resulted in additional rapid declines in HBV DNA and RNA to similar levels as subjects initially randomized to ALG-000184 + ETV.
- HBV DNA & RNA levels are consistent in N=3 and N=9 subjects, respectively.

Figure 4: Mechanism (SEM) HBV DNA Change from Baseline Over Time

CONCLUSIONS

- Untreated HBsAg positive CHB subjects given 300 mg of ALG-000184 and ETV for up to 36 weeks resulted in:
  - A favorable safety and PK profile
  - Significant reductions in HBV DNA and RNA which are superior to those seen with ETV alone.
  - Substantial HBsAg reductions in most subjects:
    - ≥ 0.5 log(10) IU/mL in 7/12 subjects dosed 12 weeks
    - ≥ 1.0 log(10) IU/mL in 47 subjects dosed 24 weeks
    - Maximum reduction observed to date: ≥ 2.0 log(10) IU/mL (Week 36)
  - Treatment in this cohort is ongoing and will evaluate if further reductions in HBsAg can be achieved with longer duration of dosing.
  - In addition, 300 mg of ALG-000184 is being evaluated as monotherapy in TINCT CHB patients, including HBsAg negative and positive subjects.
  - These results demonstrate that treatment with ALG-000184, an orally administered CAM-E, can result in multiple reductions of HBsAg confirming that it may have a direct effect on cccDNA activity. As such, ALG-000184 could be utilized as a key component of combination therapy to achieve complete suppression of HBsAg and functional cure.

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10. Employees of Aligos Therapeutics

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